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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/446,628	09/19/2001	Mihael H. Polymeropoulos	31978-164334	2655

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EXAMINER

HUNNICUTT, RACHEL KAPUST

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 11/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/446,628	Applicant(s) POLYMEROPOULOUS ET AL.	
	Examiner Rachel K. Hunnicutt	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6,10,11,24-30,33-40,44-49,57,61,75 and 76 is/are pending in the application.
- 4a) Of the above claim(s) 24-30,33-40,and 44-49 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 5,6,10,75 and 76 is/are allowed.
- 6) ☒ Claim(s) 1-4,11 and 57 is/are rejected.
- 7) ☒ Claim(s) 61 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

RESPONSE TO AMENDMENT

Applicant's amendment filed September 28, 2004 is acknowledged. Claims 7-9, 12-23, 31-32, 41-43, 50-56, 58-60, and 62-74 have been canceled. Claims 5, 6, 24, and 57 are amended. Claims 75-76 are new. Claims 24-30, 33-40, 44-49, and 75-76 are withdrawn from consideration as being drawn to non-elected inventions. New claims 75 and 76 are rejoined for the reasons stated below. Claims 1-6, 10, 11, 57, 61, 75, and 76 are under consideration. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

The rejection of claims 5 and 10 under 35 U.S.C. 112, first paragraph, for lack of enablement, is withdrawn in response to Applicants' amendments to the claims. The rejection of claims 11 and 58-59 is withdrawn in response to the cancellation of these claims.

The rejection of claims 5 and 10 under 35 U.S.C. 112, first paragraph, for not complying with the written description requirement, is withdrawn in response to Applicants' amendments to the claims. The rejection of claims 11 and 58-59 is withdrawn in response to the cancellation of these claims.

Claim Rejections Maintained/New Grounds of Rejection

Claim Objections

Claim 57 is objected to because of the following informalities: Claim 57 reads "wherein a guanine is replaced by an **alanine**", and it should read "wherein a guanine is replaced by an **adenine**". Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 11 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 11 recites "host cell comprising", which encompasses the host cell, as it occurs in nature, for example, as a gene therapy patient. However, since Applicants do not intend to claim a naturally occurring product, amendment of the claim to show the hand of man would obviate this rejection. It is suggested that claim 11 be amended to recite "an isolated host cell". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The rejection of claims 1-4 and 57 under 35 U.S.C. 112, first paragraph, for lack of enablement, is maintained for reasons of record on p. 2-4 of paper no. 0504.

Applicants argue that there are only a limited number of possible mutations at position 209, and thus a limited number of mutations to be made and used (p. 6 of response). Applicants also argue that persons of skill in the art will be able to make and use the nucleic acids of claims 1-3 without undue experimentation (p. 7 of response). Applicants refer to the teachings of Kruger *et al.* and Zarranz *et al.* which demonstrate that other missense mutations in the alpha-synuclein can cause Parkinson's disease.

Applicants' arguments have been fully considered but have not been found to be persuasive. Claims 1-3 are drawn to any nucleic acid sequence encoding a mutated human synuclein protein such as alpha, beta, or gamma synuclein or a homologue thereof. Claim 4 is drawn to a nucleic acid encoding at least one mutation at base pair position 209 of alpha synuclein. The sequence of alpha synuclein was known to the public prior to the teachings of Applicant (see NCBI Accession No. AAC02114, Xia *et al.*). Applicants' only advancement to furthering the useful arts and sciences is the disclosure of the mutation at position 209 from a

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guanine to an adenine. Applicants have taught that the G209A mutation is diagnostic for Parkinson's disease, but that is all Applicants have taught. Applicants have not taught that any other mutation in any synuclein is diagnostic for Parkinson's disease. Applicants have not taught that any other mutation at position 209 is diagnostic for Parkinson's disease.

Even though one skilled in the art could engineer a mutant synuclein, the skilled artisan would not know how to use it in order to diagnose Parkinson's disease. Similarly, the skilled artisan would not know how to use a "homolog", which is at least 25% homologous to a mutated human synuclein, in order to diagnose Parkinson's disease. The references cited by Applicants only teach that others have spent the time and effort to discover new mutations in alpha synuclein associated with Parkinson's disease. The claims of the current invention would encompass the teachings of Kruger et al. and Zarranz et al., yet the skilled artisan would not have known to use the Ala30Pro mutation or the Glu36Lys mutation for diagnosing Parkinson's disease. Applicants did not provide any guidance in the specification to suggest that these mutations would be useful in diagnosing Parkinson's disease, nor did they suggest that any mutation other than the G209A mutation would be useful in diagnosing Parkinson's disease.

Claim 57 is drawn to a nucleic acid comprising a mutation in an alpha human synuclein gene wherein a guanine is replaced by an alanine at base pair position 209. The claim reads on a single alanine, which would not be diagnostic for Parkinson's disease.

The rejection of claims 1-4 and 57 under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement, is maintained for reasons of record on p. 4-5 of paper no. 0504.

Applicants argue that the description provided in the specification is adequate to cover the limited number of variants containing a mutation at position 209 (p. 7 of response). Applicants also refer to the teachings of Kruger et al. and Zarranz et al. to demonstrate that other missense mutations in the alpha-synuclein gene can cause Parkinson's disease (p. 8 of response).

As previously stated, the instant disclosure of one mutant human alpha-synuclein does not adequately describe the scope of the claimed genus, which encompasses hundreds upon hundreds of different nucleic acid sequences. Although other mutations in the alpha-synuclein

gene can cause Parkinson's disease, the specification does not describe such mutations. The specification does not mention the Ala30Pro mutation or the Glu36Lys mutation. The skilled artisan would not recognize that Applicants were in possession of such mutations at the time of the filing of the application, yet these mutations would be within the genus of the claimed invention. Similarly, although there are a limited number of variants that contain a mutation at position 209, only the G209A mutation is diagnostic for Parkinson's disease. The skilled artisan would not be able to predictably identify the encompassed molecules as being diagnostic for Parkinson's disease, and the skilled artisan would not recognize Applicants being in possession of any mutation other than the G209A mutation of alpha synuclein.

Conclusion

Claims 5, 6, and 10 are allowed. In view of claims 5, 6, and 10 being allowed, dependent claims 75 and 76 are rejoined. Claims 75 and 76 are also allowed.

Claim 61 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 1-4, 11, and 57 are rejected.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel K. Hunnicutt whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RKH

11/16/04


JANET ANDRES
PRIMARY EXAMINER